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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,293	06/27/2003	Matthew James Callow	CAL-1CIP	9024

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NUVELO, INC
201 INDUSTRIAL ROAD
SUITE 310
SAN CARLOS, CA 94070

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/608,293	CALLOW ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Claims 1-22 are pending. Claims 18-22 are under examination. Claims 1-17 are withdrawn as being directed to non-elected subject matter. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 18-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Fodor et al. (US 2001/0053519).

With regard to claim 18, Fodor et al. teach two sets of universal building blocks comprising:

a) a first set of single-stranded oligonucleotides having a first end and a second end, said first end having a sticky-end overhang and said second end having sequence of 8-20 bases; and

b) a second set of single-stranded oligonucleotides having a first end and a second end said first end having a sticky-end overhang and said second end having a sequence of 8-20 bases, wherein said first ends of said first and second sets are different, and said second end of said first set are

complementary to said second end of said second set, generating all possible combinations of adapter sequences (see paragraph 0122, where Fodor et al teach making all possible 10 mers. The 10 mers necessarily encompass the instantly claimed oligonucleotide sets. Here the 10 mers comprise ALL POSSIBLE 10 mers this set of 10mers, comprising 4^{10} different sequences, will necessarily have oligonucleotides found within the instantly claimed sets. Admittedly, there will also be 10mers present in the set which do not meet the structural limitations of the instantly claimed oligos but Applicant uses the language of comprising so the reference is allowed to encompasses these additional elements).

With regard to claim 19, Fodor et al. teach the sets of universal building blocks of claim 18, wherein said first and second set are comprised of up to 64 different first end 3-base overhangs (see paragraph 0122, where Fodor et al teach making all possible 10 mers. All possible 10 mers necessarily encompass the instantly claimed oligonucleotide sets. All possible 10mers will necessarily comprise all possible overhangs, for example all possible 1 base overhangs, 2 base overhangs 3 base overhangs, 4 base overhangs and 5 base overhangs).

With regard to claim 20, Fodor et al. teach the sets of universal building blocks of claim 18, wherein said first and second set are comprised of up to 256 different first end 4-base overhangs (see paragraph 0122, where Fodor et al teach making all possible 10 mers. All possible 10 mers necessarily encompass the instantly claimed oligonucleotide sets).

With regard to claim 21, Fodor et al. teach the sets of universal building blocks of claim 18, wherein said first and second set are comprised of up to 1024 different first end 5-base overhangs (see paragraph 0122, where Fodor et al teach making all possible 10 mers. All possible 10 mers necessarily encompass the instantly claimed oligonucleotide sets).

With regard to claim 22, Fodor et al. teach the adaptor sequences generated from hybridization of oligonucleotides in the first set to oligonucleotides in the second set are in an amount equal to the number of oligonucleotides in the first set multiplied by the number of oligonulceotides in the second set

(see paragraph 0122, where Fodor et al teach making all possible 10 mers. All possible 10 mers necessarily encompass the instantly claimed oligonucleotide sets).

3. Claims 18-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ichikawa et al. (PNAS 2000).

With regard to claim 18, Ichikawa et al. teach two sets of universal building blocks comprising:

a) a first set of single-stranded oligonucleotides having a first end and a second end, said first end having a sticky-end overhang and said second end having sequence of 8-20 bases; and

b) a second set of single-stranded oligonucleotides having a first end and a second end said first end having a sticky-end overhang and said second end having a sequence of 8-20 bases, wherein said first ends of said first and second sets are different, and said second end of said first set are complementary to said second end of said second set, generating all possible combinations of adapter sequences (see p. 9660 col. 2 under RT-PCR analysis line 4, where Ichikawa et al teach random decamers. The random decamers necessarily encompass the instantly claimed oligonucleotide sets. Here the random decamers comprise ALL POSSIBLE 10mers this set of 10mers, comprising 4^{10} different sequences, will necessarily have oligonucleotides found within the instantly claimed sets. Admittedly, there will also be 10mers present in the set which do not meet the structural limitations of the instantly claimed oligos but Applicant uses the language of comprising so the reference is allowed to encompasses these additional elements).

With regard to claim 19, Ichikawa et al. teach the sets of universal building blocks of claim 18, wherein said first and second set are comprised of up to 64 different first end 3-base overhangs (see p. 9660 col. 2 under RT-PCR analysis line 4, where Ichikawa et al teach random decamers. The random decamers necessarily encompass the instantly claimed oligonucleotide sets. All possible 10mers will

necessarily comprise all possible overhangs, for example all possible 1 base overhangs, 2 base overhangs 3 base overhangs, 4 base overhangs and 5 base overhangs).

With regard to claim 20, Ichikawa et al. teach the sets of universal building blocks of claim 18, wherein said first and second set are comprised of up to 256 different first end 4-base overhangs (see p. 9660 col. 2 under RT-PCR analysis line 4, where Ichikawa et al teach random decamers. The random decamers necessarily encompass the instantly claimed oligonucleotide sets).

With regard to claim 21, Ichikawa et al. teach the sets of universal building blocks of claim 18, wherein said first and second set are comprised of up to 1024 different first end 5-base overhangs (see p. 9660 col. 2 under RT-PCR analysis line 4, where Ichikawa et al teach random decamers. The random decamers necessarily encompass the instantly claimed oligonucleotide sets).

With regard to claim 22, Ichikawa et al. teach the adaptor sequences generated from hybridization of oligonucleotides in the first set to oligonucleotides in the second set are in an amount equal to the number of oligonucleotides in the first set multiplied by the number of oligonulceotides in the second set (see p. 9660 col. 2 under RT-PCR analysis line 4, where Ichikawa et al teach random decamers. The random decamers necessarily encompass the instantly claimed oligonucleotide sets).

Response to Arguments

3. Applicants' arguments filed March 14, 2007, have been fully considered but they are not persuasive.

With regard to the 102 (b) rejection over all the claims, Applicants argue in a truly random set of 10 base oligos, the possibility exists that each and every sequence in the population is exactly the same. This argument is not persuasive because while the possibility exists its literally is infinitesimal. For example if sequence 1 is sequence X the chance that sequence 2 will also be X is 1 in 4^{10}. The chance that sequence 3 will also be X is $(1 \text{ in } 4^{10})^2$. Ichikawa discloses obtaining decamers from Ambion. These

random decamers are at a concentration of 50 μM in a volume of 80 μL. This solution of random decamers contains 2.408×10^{15} moleucles, therefore the likelihood that all of these molecules are the same is $(1 \text{ in } 4^{10})^{(2.408 \times 1015)}$. In this solution of random decamers there is 2.4×10^{9} moleucles for *each* 10 mer. There will be some sequences which will be exactly the same, however to assert all of the sequences will be exactly the same is mathematically ridiculous. Additionally, Ambion will not sell random decamers if the oligonucleotides all have identical sequences. Applicants argue because Ichikawa does not disclose specific sequence data for the random 10 mers there is no evidence as to the structure of the oligos found in the random set. This argument is not persuasive because the specific sequence data is unnecessary. The only structural limitation recited in the instant claims is the requirement that each oligonucleotide be single stranded.

Finally, Applicants argue claim 1 is directed to two sets of oligonucleotides which are not mixed. This argument is not persuasive because the claims recite nothing to indicate the sets are not mixed. Further Applicants do not define set so a set could encompass 2 oligos, 6 oligos, 600 oligos etc. Ichikawa teaches random decamers. Random decamers comprise comprising 4^{10} different sequences which can be divided into sets of 2 oligos, 6oligos, 600 oligos etc.

Summary

4. No claims were allowed.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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